L7 ANSWER 26 OF 42 MEDLINE
AN 96001935 MEDLINE
DN 96001935 PubMed ID: 8580262
TI In **vitro** biocompatibility testing of polymers for orthopaedic implants using cultured fibroblasts and osteoblasts.
AU Morrison C; Macnair R; MacDonald C; Wykman A; Goldie I; Grant M H
CS Bioengineering Unit, University of Strathclyde, Wolfson Centre, Glasgow, UK.
SO BIOMATERIALS, (1995 Sep) 16 (13) 987-92.
Journal code: 8100316. ISSN: 0142-9612.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199603
ED Entered STN: 19960327
Last Updated on STN: 19980206
Entered Medline: 19960320
AB The biocompatibility of two polymers for potential use as orthopaedic implant materials in an isoelastic hip prosthesis was investigated. The interactions of polyetheretherketone (PEEK) and epoxy resin polymers (with and without carbon fibre reinforcement) with both fibroblasts and osteoblasts were tested using cell protein, intracellular reduced glutathione (GSH), leakage of **lactate dehydrogenase** and the **MTT assay** as indices of cellular **cytotoxicity**. The epoxy resin polymer was slightly cytotoxic to and inhibited the growth rate of fibroblasts (as assessed by total cell protein), and depleted GSH in both cell types. In contrast, the PEEK material did not display overt signs of **cytotoxicity** and, in fact, increased osteoblast cell protein content. This suggests that, of these two materials, PEEK would be the one of choice for development of an isoelastic implant and, in view of its stimulatory effect on osteoblast protein content, it may encourage ingrowth of bone around the prosthesis and thus minimize joint loosening.

L7 ANSWER 38 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 9
AN 1992:396269 BIOSIS
DN BA94:68444
TI **TOXICITY** ASSESSMENT OF TOXINS T-514 AND T-544 OF BUCKTHORN KARWINSKIA-HUMBOLDTIANA IN PRIMARY SKIN AND LIVER **CELL CULTURES**.
AU GARZA-OCANAS L; HSIEH G C; ACOSTA D; TORRES-ALANIS O; PINEYRO-LOPEZ A
CS DEP. FARMACOL. TOXICOL., FAC. MED., UNIV. AUTONOMA NEUVO LEON, APARTADO POSTAL 146, COLONIA DEL VALLE, NUEVO LEON, MEXICO.
SO TOXICOLOGY, (1992) 73 (2), 191-201.
CODEN: TXCYAC. ISSN: 0300-483X.
FS BA; OLD
LA English
AB The present study was undertaken to assess and compare the in **vitro cytotoxicity** of toxins T-514 and T-544 of buckthorn (Karwinskia humboldtiana) using primary **cultures** of rat hepatocytes and keratinocytes. **Cell cultures** were exposed to 6, 12, 25 and 50 .mu.M toxins for 2-, 4-, 6- and 24-h periods. **Cytotoxicity** was determined by release of the cytoplasmic enzyme, **lactate dehydrogenase** (LDH), in culture media, methylthiazoltetrazolium (**MTT**) reduction and neutral red (NR) uptake. An increase in LDH leakage was observed in liver **cell cultures** as early as 2 h with 50 .mu.M T-544 and with 6 .mu.M T-514 and T-544 at 6 h and 24 h, respectively. In the NR **assay** the **toxicity** was evident at 2 h with 12 .mu.M T-514 and T-544 and with 6 .mu.M concentrations of both toxins at 6 h. On the other hand, a decrease in **MTT** reduction was detected at 4 h with 50 .mu.M concentrations of both toxins and with 25 .mu.M T-544 and 12 .mu.M T-514 at 6 h and 6 .mu.M T-514 and T-544 at 24 h. Both toxins were shown to be highly hepatotoxic; T-514 was more toxic than T-544. In the skin **cell cultures**, the **toxicity** of the toxins was not as severe and was not expressed until 12 h of exposure.

L7 ANSWER 39 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 10
AN 1993:147887 BIOSIS
DN PREV199395080687
TI Evaluation of surfactant **cytotoxicity** potential by primary cultures of ocular tissues: I. Characterization of rabbit corneal epithelial cells and initial injury and delayed **toxicity** studies.
AU Grant, Roberta L.; Yao, Cheng; Gabaldon, Donna; Acosta, Daniel (1)
CS (1) Dep. Pharmacol./Toxicol., Coll. Pharmacy, Univ. Tex. Austin, Austin, Tex. 78712 USA
SO Toxicology, (1992) Vol. 76, No. 2, pp. 153-176.
ISSN: 0300-483X.
DT Article
LA English
AB This investigation was undertaken to develop **cytotoxicity** **assay** systems using primary **cultures** of rabbit corneal epithelial **cells** as an experimental model to evaluate oculotoxic agents and the ability of these in **vitro assay** systems to predict irritancy potential and delayed **toxicity**. We have characterized the epithelial nature of the cultures by identifying keratins with antikeratin antibodies (AE1/AE3) and by demonstrating metabolic enzymes important to the integrity of the cells: **lactate dehydrogenase**, glucose 6-phosphate dehydrogenase and aldolase. Eight surfactants were compared and ranked according to their cytotoxic potential. We evaluated **cytotoxicity** by measuring leakage of the cytosolic enzyme, **lactate dehydrogenase**, into the medium, by making morphological observations and by assessing lysosomal neural red uptake and mitochondrial 3-(4,5-dimethythiazol-2-yl)-2,5-

L7 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2003 ACS
AN 1992:646649 CAPLUS
DN 117:246649
TI Surfactant **cytotoxicity** potential evaluated with primary cultures of ocular tissues: a method for the **culture** of rabbit conjunctival epithelial **cells** and initial **cytotoxicity** studies
AU Yao, C.; Acosta, D.
CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA
SO Toxicology Methods (1992), 2(3), 199-218
CODEN: TOMEEB; ISSN: 1051-7235
DT Journal
LA English
AB In order to rank the irritancy potential of chems. objectively and biochem., a primary **culture** method for rabbit conjunctival epithelial **cells** was developed as a potential in **vitro** method for ocular **toxicity** testing of xenobiotics. Conjunctival epithelial cells were dispersed by Dispase II, followed by trypsin treatment. **Cells** were **cultured** in serum-free medium of 1:1 ratio of Dulbecco's modified Eagle's medium (DMEM) and F-12 nutrient mixt. plus various concns. of growth factors. At a plating d. of 85,000 cells/cm2, cells grew to confluency in 3-4 days. Conjunctival cells showed a pos. anti-keratin antibody stain which demonstrated their epithelial nature. These cells also showed pos. periodic acid-Schiff (PAS) staining which is consistent with their goblet cell-contg. and mucin-secreting function in vivo. Three surfactants, benzalkonium chloride (BzCl), sodium dodecyl sulfate (SDS), and Tween 20 (T-20; polyoxyethylene sorbitan monolaurate), at concns. 2-20, 10-50, and 200-1500 .mu.g/mL, resp., were evaluated for their **cytotoxicity** potential. Cell injury was assessed by **lactate dehydrogenase** (LDH) leakage (cell membrane integrity), uptake of neutral red (NR) (lysosomal homeostasis), and the redn. of 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyltetrazolium bromide (**MTT**) (mitochondrial metabolic activity). The potential for causing cell injury was uniformly in the order of BzCl > SDS .mchgt. T-20 in the three **assays** (estd. EC50 values for BzCl, SDS, and T-20 were 25, 50, and 1585 .mu.g/mL for LDH; 6, 25, and 794 .mu.g/mL for NR; and 8, 40, and 1259 .mu.g/mL for **MTT**, resp.). These results correlate well with reported results of the Draize eye irritancy test in vivo and suggest that a model of primary **culture** of rabbit conjunctival epithelial **cells** may be useful in predicting the eye irritancy potential of surfactants.

L5 ANSWER 157 OF 164 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1991:116361 BIOSIS
DN BA91:63751
TI A STUDY ON THE **CYTOTOXICITY** OF ADRIAMYCIN ON **CULTURED** RAT MYOCARDIAL AND ENDOTHELIAL **CELLS**.
AU CHUNG Y T; CHOI M K; KIM J J; KIM J M; PARK S T
CS DEP. ANATOMY, WONKWANG UNIV. MED. SCH., IRI, KOREA.
SO CHONNAM J MED SCI, (1988) 1 (2), 128-138.
CODEN: CJMSEZ.
FS BA; OLD
LA English
AB To evaluate the **cytotoxicity** of adriamycin, cellular uptake of neutral red (NR) and tetrazolium (MTT), lactate dehydrogenase (LDH) activity and protein content were determined on **cultured** myocardial and endothelial **cells** from the heart of the newborn rat. Light and electron microscopic studies were also carried out. Initial and midpoint cytotoxicities of adriamycin in myocardial cells were at lower concentrations in the NR **assay** (NR90, 0.07 .mu.g/ml; NR50, 2.0 .mu.g/ml) than in the MTT **assay** (MTT90, 0.15 .mu.g/ml; MTT50, 2.8 .mu.g/ml). However, in endothelial cells, they were at lower concentrations in the MTT **assay** (MTT90, 0.1 .mu.g/M1; MTT50; 2.3 .mu.g/ml) than in the NR **assay** (NR90, 0.3 .mu.g/ml; NR50, 4.1 .mu.g/ml). Protein contents in myocardial cells treated with adriamycin at NR50 and MTT50 were 38.1% and 34.1%, respectively, of the control, and those in endothelial cells were 36.4% and 45.7% of the control, respectively. Adriamycin increased the amount of LDH in both myocardial and endothelial cells, depending on the dose of adriamycin. Light microscopy revealed that both myocardial and endothelial cells treated with adriamycin decreased in number of cells and that the cells became more spherical compared to the control. Electron microscopy of adriamycin-treated cells showed increments in lysosomes and vacuoles along with swelling of **mitochondria** and cisternal dilation of rough endoplasmic reticulum. These results suggest that adriamycin inhibits in **vitro** proliferation and growth of the cells by disturbing the cell metabolism.

L18 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:60983 CAPLUS
DN 137:163397
TI Experimental study of mustine and its isomeride on tumor
AU Ren, Min
CS Department of Hematology, People's Hospital of Qinghai Province, Qinghai, 810007, Peop. Rep. China
SO Tianjin Yiyao (2001), 29(12), 724-726
CODEN: TIYADG; ISSN: 0253-9896
PB Tianjin Yixue Zazhishe
DT Journal
LA Chinese
AB The effects of mustine and its isomeride on K562 and L1210 cell lines were studied. Clone assay, MTT colorimetric assay and survival cell count assay were adopted. Mustine and its isomeride had inhibitory effects on K562 and L1210 cells. The inhibition effects in expt. groups were more obvious than that in control group ($P<0.01$). There was a pos. correlation between drug concn. and inhibitory rates. Isomeride of mustine has a stronger inhibitory effect on K562 and L1210 cells than mustine.

L7 ANSWER 16 OF 42 MEDLINE
AN 1999229948 MEDLINE
DN 99229948 PubMed ID: 10215109
TI Influence of uranium(VI) speciation for the evaluation of in **vitro** uranium **cytotoxicity** on LLC-PK1 cells.
AU Mirto H; Barrouillet M P; Henge-Napoli M H; Ansoborlo E; Fournier M; Cambar J
CS Institut de Protection et de Surete Nucleaire, Departement de Protection de la sante de l'Homme et de Dosimetrie, Pierrelatte, France.
SO HUMAN AND EXPERIMENTAL TOXICOLOGY, (1999 Mar) 18 (3) 180-7.
Journal code: 9004560. ISSN: 0960-3271.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
ED Entered STN: 19990618
Last Updated on STN: 19990618
Entered Medline: 19990607
AB Very few data are available concerning the in **vitro** **toxicity** of uranium. In this work, we have determined the experimental chemical conditions permitting the observation of uranium(VI) **cytotoxicity** on LLC-PK1 cells. Uranium solutions made either by dissolving uranyl acetate or nitrate crystals, or by complexing uranium with bicarbonate, phosphate or citrate ligands, were prepared and tested. Experiments demonstrated that only uranium solutions containing citrate and bicarbonate ligands concentrations tenfold higher than the metal, were soluble in the **cell culture** medium.
Cytotoxicity studies of all these uranium compounds were performed on LLC-PK1 cells and compared using LDH release, neutral red uptake and **MTT assays**. Dose dependent **cytotoxicity** curves were only obtained with uranium-bicarbonate medium. This study has revealed a **toxicity** of uranium-bicarbonate complexes for 24 h expositions and for concentrations ranging from 7 x 10(-4)-10(-3) M, under these conditions, the CI50 (**cytotoxicity** index) was evaluated between 8.5 and 9 x 10(-4) M. In contrast, we noticed a lack of **cytotoxicity** response for uranium(VI)-citrate complexes. Electron transmission microscopy studies revealed, when LLC-PK1 cells were exposed to the uranium-bicarbonate system, that uranium penetrated and precipitated within the cytoplasmic compartment. Morphological studies conducted with citrate complexes did not show any cellular intake of uranium.

(FILE 'HOME' ENTERED AT 06:45:15 ON 11 AUG 2003)

FILE 'BIOSIS, MEDLINE, INPADOC, CAPLUS' ENTERED AT 06:45:27 ON 11 AUG 2003

L1	52404	GLUTATHIONE(5A)TRANSFERASE
L2	354150	ATP
L3	16343	MTT
L4	604	ALAMAR BLUE
L5	0	L1 AND L2 AND L3 AND L4
L6	1038	L1 AND L2
L7	1	L6 AND L3
L8	4	L4 AND L1
L9	228	L1 AND L2 AND ASSAY?
L10	19	L9 AND (TOXIC? OR CYTOTOXIC?)
L11	10	DUPLICATE REMOVE L10 (9 DUPLICATES REMOVED)
L12	2214	(COUNT?(5A)CELL?) AND ASSAY? AND (TOXIC? OR CYTOTOXIC?)
L13	8	L1 AND L12
L14	592	ATP ASSAY
L15	53	L3 AND L4
L16	29	DUPLICATE REMOVE L15 (24 DUPLICATES REMOVED)
L17	30	CELL COUNT ASSAY
L18	17	DUPLICATE REMOVE L17 (13 DUPLICATES REMOVED)
L19	142	L1 AND L3
L20	1	L19 AND L4
L21	5	L2 AND L3 AND L4
L22	0	L1 AND L2 AND L4
L23	16	L2 AND L4
L24	9	DUPLICATE REMOVE L23 (7 DUPLICATES REMOVED)

=>

(FILE 'HOME' ENTERED AT 07:54:57 ON 11 AUG 2003)

FILE 'BIOSIS, MEDLINE, INPADOC, CAPLUS' ENTERED AT 07:55:06 ON 11 AUG 2003

L1 0 (GLUTATHIONE(3A)TRANSFERASE) AND (ATP(3A)ASSAY?) AND (CELL?(3A)
L2 2 (GLUTATHIONE(3A)TRANSFERASE) AND (ATP) AND (CELL?(3A)COUNT?)
L3 592 ATP ASSAY
L4 52272 (GLUTATHIONE(3A)TRANSFERASE)
L5 0 L3 AND L4

=>

=>

L Numb r	Hits	Search Text	DB	Time stamp
1	70	mtt and atp and alamar and glutathi n	USPAT; US-P PUB; EPO; JPO; DERWENT	2003/08/11 07:51
2	2	glutathione same (cell adj3 count) same ATP	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/11 07:52

L5 ANSWER 161 OF 164 CAPLUS COPYRIGHT 2003 ACS
AN 1987:419079 CAPLUS
DN 107:19079
TI Extracellular release of enzymes from macrophages in **vitro** for measuring cellular interaction with particulate and non-particulate materials
AU Lock, S. O.; Jones, P. A.; Friend, J. V.; Parish, W. E.
CS Environ. Saf. Lab., Unilever Res. Eng., Bedford, MK44 1LQ, UK
SO Toxicology in Vitro (1987), 1(2), 77-83
CODEN: TIVIEQ; ISSN: 0887-2333
DT Journal
LA English
AB Mammalian **cells** in **culture** provide a sensitive and rapid in **vitro** test for the study of many aspects of **toxicity** impractical in vivo. **Assays** have been established for 8 enzymes used as markers for different subcellular locations (plasma membrane, cytoplasm, **mitochondria** and lysosomes). The time-course and dose-response relationships of enzyme release from macrophages exposed to a series of toxic and nontoxic mineral dusts and sol. detergents have been examd. The different patterns of extracellular enzyme release illustrate the basic mechanisms of cell damage, covering nontoxic interactions (little or no enzyme release except at very high concns.), immediate **cytotoxicity** (lysosomal and cytoplasmic enzyme release at similar rates, with the majority of enzyme release occurring with the 1st 4 h), delayed **cytotoxicity** (lysosomal and cytoplasmic enzyme release at similar rates increasing exponentially over 17 h), phagocytic release/activation (selective release of lysosomal enzymes in the absence of cytoplasmic enzymes) and membranolytic interaction (selective release of cytoplasmic enzymes with relatively little lysosomal enzyme release). Enzyme release from macrophages in **vitro** can provide information about the site and nature of cytotoxic interactions.

L7 ANSWER 39 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 10
AN 1993:147887 BIOSIS
DN PREV199395080687
TI Evaluation of surfactant **cytotoxicity** potential by primary cultures of ocular tissues: I. Characterization of rabbit corneal epithelial cells and initial injury and delayed **toxicity** studies.
AU Grant, Roberta L.; Yao, Cheng; Gabaldon, Donna; Acosta, Daniel (1)
CS (1) Dep. Pharmacol./Toxicol., Coll. Pharmacy, Univ. Tex. Austin, Austin, Tex. 78712 USA
SO Toxicology, (1992) Vol. 76, No. 2, pp. 153-176.
ISSN: 0300-483X.
DT Article
LA English
AB This investigation was undertaken to develop **cytotoxicity assay** systems using primary **cultures** of rabbit corneal epithelial **cells** as an experimental model to evaluate oculotoxic agents and the ability of these in **vitro assay** systems to predict irritancy potential and delayed **toxicity**. We have characterized the epithelial nature of the cultures by identifying keratins with antikeratin antibodies (AE1/AE3) and by demonstrating metabolic enzymes important to the integrity of the cells: **lactate dehydrogenase**, glucose 6-phosphate dehydrogenase and aldolase. Eight surfactants were compared and ranked according to their cytotoxic potential. We evaluated **cytotoxicity** by measuring leakage of the cytosolic enzyme, **lactate dehydrogenase**, into the medium, by making morphological observations and by assessing lysosomal neural red uptake and mitochondrial 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyl tetrazolium bromide (**MTT**) reduction. The cells were treated for 1 h with the surfactants and the possibility of delayed **toxicity** was evaluated 24 h after removal of the surfactant. The **cytotoxicity** of the different types of surfactants as shown by all the tests was cationic gt anionic = amphoretic gt non-ionic. Triton X-100, a non-ionic surfactant but a severe irritant, had a ranking similar to anionic surfactants. The in **vitro** rankings corresponded well to reported in vivo Draize rabbit eye test data. The 24-h test for **lactate dehydrogenase** leakage showed that mild and non-irritating surfactants did not demonstrate any subsequent damage after a 1-h exposure, but the extreme and severe surfactants continued to show further damage after the 1-h exposure. These in **vitro** findings were similar to reported in vivo results. The neural red and **MTT** tests did not adequately predict the prolonged **toxicity** of the more irritating surfactants, as was demonstrated by the **lactate dehydrogenase** leakage test. We conclude that in **vitro cytotoxicity assays** using primary **cultures** of rabbit corneal epithelial **cells** may be used to rank the cytotoxic potential of surfactants, but only the **lactate dehydrogenase** leakage test was able to assess prolonged cell injury.

L7 ANSWER 40 OF 42 MED

ANSWER 41 OF 42 MEDLINE

AN 92069305 MEDLINE

DN 92069305 PubMed ID: 1958848

TI Comparison of **cytotoxicity** in heart cells and tumor cells exposed to DNA intercalating agents in **vitro**.

AU Dorr R T; Shipp N G; Lee K M

CS University of Arizona, Pharmacology Department, Tucson.

NC CA 17094 (NCI)
CA 23078 (NCI)
CA 49875 (NCI)

SO ANTI-CANCER DRUGS, (1991 Feb) 2 (1) 27-33.
Journal code: 9100823. ISSN: 0959-4973.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199201

ED Entered STN: 19920124
Last Updated on STN: 19970203
Entered Medline: 19920108

AB A new approach to antitumor analog selection was evaluated using in **vitro cytotoxicity assays** in tumor cells and heart cells. Eight anthracycline antibiotics and five non-anthracycline DNA intercalating agents were separately exposed to human 8226 myeloma cells and neonatal rat heart myocytes in **vitro**. Survival was measured after six days of culture by the **MTT** dye method for tumor cells and by ATP content for heart cells. Inhibitory drug concentrations in 50% of cells (IC50) were determined from log-linear dose-response curves for each agent. The IC50 values in the tumor cells ranged from 0.002 micrograms/ml for idarubicin to 3.5 micrograms/ml for the primary metabolite of doxorubicin, doxorubicinol. In contrast, IC50 values for anthracyclines in rat heart cells averaged approximately 357-fold higher than in the tumor cells. The heart cell/tumor IC50 ratio was 114.4 for the parent anthracycline doxorubicin. Compounds with poor cytotoxic selectivity for tumor cells included doxorubicinol, amonafide, amsacrine and bisantrene. Compounds with reduced cardiotoxicity included the anthracyclines daunorubicin (IC50 ratio of 550), esorubicin (IC50 ratio of 1500) and the anthracene derivative mitoxantrone (IC50 ratio of 500). These results show that simultaneous comparisons of **cytotoxicity** in heart cells and tumor cells can identify agents such as daunorubicin and mitoxantrone which are known to produce less cardiac **toxicity** in vivo. With further testing, this methodology may be applicable to preclinical screening programs to select active DNA intercalating agents with low cardiotoxic potential.

L7 ANSWER 42 OF 42 BIOSIS COPYRI

diphenyl tetrazolium bromide (**MTT**) reduction. The cells were treated for 1 h with the surfactants and the possibility of delayed **toxicity** was evaluated 24 h after removal of the surfactant. The **cytotoxicity** of the different types of surfactants as shown by all the tests was cationic gt anionic = amphoretic gt non-ionic. Triton X-100, a non-ionic surfactant but a severe irritant, had a ranking similar to anionic surfactants. The in **vitro** rankings corresponded well to reported in vivo Draize rabbit eye test data. The 24-h test for **lactate dehydrogenase** leakage showed that mild and non-irritating surfactants did not demonstrate any subsequent damage after a 1-h exposure, but the extreme and severe surfactants continued to show further damage after the 1-h exposure. These in **vitro** findings were similar to reported in vivo results. The neural red and **MTT** tests did not adequately predict the prolonged **toxicity** of the more irritating surfactants, as was demonstrated by the **lactate dehydrogenase** leakage test. We conclude that in **vitro** **cytotoxicity assays** using primary **cultures** of rabbit corneal epithelial **cells** may be used to rank the cytotoxic potential of surfactants, but only the **lactate dehydrogenase** leakage test was able to assess prolonged cell injury.

L7 ANSWER 40 OF 42 MEDLINE

2002:806848 CAPLUS
DN 138:348542
TI Differential in vitro hepatotoxicity of troglitazone and rosiglitazone among cryopreserved human hepatocytes from 37 donors
AU Lloyd, Scott; Hayden, Michael J.; Sakai, Yumiko; Fackett, Andrew; Silber, Paul M.; Hewitt, Nicola J.; Li, Albert P.
CS In Vitro Technologies, Inc., Baltimore, MD, 21227, USA
SO Chemico-Biological Interactions (2002), 142(1-2), 57-71
CODEN: CBINA8; ISSN: 0009-2797
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB The authors report here on their studies on troglitazone and rosiglitazone cytotoxicity in human hepatocytes isolated from multiple donors to investigate factors responsible for individual differences in sensitivity to the known hepatotoxicity of these antidiabetic drugs. Using cellular **ATP** content as an endpoint, cytotoxicity of both drugs was evaluated in cryopreserved human hepatocytes from 37 donors. The authors confirmed reports of others that troglitazone was cytotoxic to human hepatocytes using cellular **ATP** content as an endpoint. In addn., the authors found that rosiglitazone, although less toxic in the study population, was cytotoxic to hepatocytes in some donors (EC50<100 .mu.M). **ATP** content, 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (**MTT**) metab., depletion of intracellular glutathione, **Alamar Blue** metab., and neutral red uptake were used as endpoints in a single donor study using freshly isolated human hepatocytes. Troglitazone appeared to be more toxic than rosiglitazone by all endpoints. From the demog. data provided to us for each donor, the authors were able to establish no direct correlation between cytotoxicity (expressed as EC50 values) and age, sex, smoking status, or alc. consumption. The authors conclude that troglitazone and rosiglitazone are differentially toxic to human hepatocytes, and that toxicity may be independent of age, sex, tobacco use, and alc. use.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 26 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 15
AN 1996:282402 BIOSIS
DN PREV199699004758
TI Measurement of tomatine content in tomatoes with bioassay procedure.
AU Asano, Masahiro (1); Shirota, Kouji; Anan, Toyomasa; Yamashoji, Shiro; Isshiki, Kenji (1)
CS (1) Natl. Food Res. Inst., 2-1-2 Kannondai, Tukuba, Ibaraki 305 Japan
SO Journal of the Japanese Society for Food Science and Technology, (1996) Vol. 43, No. 3, pp. 275-280.
ISSN: 0029-0394.
DT Article
LA Japanese
SL Japanese; English
AB A bioassay procedure of tomatine was examined with animal cell cultures. To detect tomatine, cytotoxicity assay procedures were applied. Cell lines of HepG 2, HuH 6KK and NIH 3T3 were suitable for this purpose, but those of HL 60 and U 937 were not. As cytotoxicity detection procedure, **alamar blue** reduction, chemiluminescence, **MTT** reduction, WST-1 reduction and others were examined. The combination of HepG 2 cell and chemiluminescence method was more suitable for detecting tomatine than any other ones. It took for 75 min to detect tomatine, and the detection limit was 2.5 mg/kg fresh weight. From unripe tomato, 353 mg/kg of tomatine was detected. From ripe tomato, 5.42 mg/kg of tomatine was detected. Tomatine content decreased as tomato fruit became ripe. Wild type tomatoes such as L. hirsutum and L. peruvianum showed high tomatine contents. Tomatoes and tomato products on the market showed low tomatine contents. A tomato, introduced tobacco mosaic virus resistant factor with genetic engineering, was planted and its tomatine content was determined. The tomatine content of the recombinant tomato was the same level as that of its host tomato.

L7 ANSWER 27 OF 42 MEDLINE
AN 95269361 MEDLINE
DN 95269361 PubMed ID: 7750192
TI Thyroid cell survival in coculture with autologous peripheral or intrathyroidal lymphocytes.
AU Massart C; Gibassier J; Le Gall F; Raoul M L; Beurtin F; Genetet B; Lucas C
CS Laboratoire de Biochimie A, CHU de Pontchaillou, Rennes, France.
SO CLINICAL ENDOCRINOLOGY, (1995 Apr) 42 (4) 379-87.
Journal code: 0346653. ISSN: 0300-0664.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199506
ED Entered STN: 19950629
Last Updated on STN: 19950629
Entered Medline: 19950619
AB OBJECTIVE: We have studied lymphocyte induced **cytotoxicity** and the production of interferon gamma (IFN-gamma) and tumour necrosis factor alpha (TNF-alpha) during coculture of thyrocytes and autologous lymphocytes from patients with Graves' disease and from normal subjects. PATIENTS: Thyroid tissues and lymphocytes were obtained from 28 patients with Graves' disease and from 9 control subjects. MEASUREMENTS: Lymphocyte induced **cytotoxicity** was evaluated on autologous thyrocytes using 5 metabolic tests: the **MTT assay**, the neutral red uptake, **lactate dehydrogenase** measurement and glutathione **assay**. IFN-gamma and TNF-alpha measurements were performed after 1, 5 or 7 days' coculture. RESULTS: The lymphocytes isolated from peripheral blood (PB lymphocytes) altered the morphology and the metabolism of autologous thyrocytes. The intrathyroidal lymphocytes isolated after Dispase digestion were not toxic whereas mechanically isolated lymphocytes exerted a little **toxicity**. No difference was seen between Graves' disease and normal cells. The supernatants from cocultures had higher IFN-gamma levels than those from lymphocyte cultures. In coculture, PB lymphocytes secreted more IFN-gamma and TNF-alpha than intrathyroidal lymphocytes. The PB lymphocyte induced **cytotoxicity** was not due to IFN-gamma and TNF-alpha alone. CONCLUSION: Peripheral blood lymphocytes are cytotoxic in **vitro** to autologous thyrocytes whereas intrathyroidal lymphocytes exert little or no **cytotoxicity** according to their isolation method. The mechanisms of lymphocyte induced **toxicity** remain to be explained.

L7 ANSWER 28 OF 42 MEDLINE
AN 96051403 MEDLINE
DN 96051403 PubMed ID: 7497906
TI Protective effect of nifedipine against **cytotoxicity** and intracellular calcium alterations induced by acetaminophen in rat hepatocyte cultures.
AU Ellouk-Achard S; Mawet E; Thibault N; Dutertre-Catella H; Thevenin M; Claude J R
CS Universite Rene Descartes--Paris V, Faculte de Pharmacie, Laboratoire de Toxicologie.
SO DRUG AND CHEMICAL TOXICOLOGY, (1995 May-Aug) 18 (2-3) 105-17.
Journal code: 7801723. ISSN: 0148-0545.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

L7 ANSWER 32 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7
AN 1994:219492 BIOSIS
DN PREV199497232492
TI An approach for development of alternative test methods based on mechanisms of skin irritation.
AU Osborne, R.; Perkins, M. A.
CS Procter and Gamble Co., Human Environ. Safety Div., Miami Valley Lab., Cincinnati, OH 45239-8707 USA
SO Food and Chemical Toxicology, (1994) Vol. 32, No. 2, pp. 133-142. ISSN: 0278-6915.
DT Article
LA English
AB Recent advances in techniques for **culture** of human skin **cells** have led to their potential for use as in **vitro** models for skin irritation testing to augment or replace existing rabbit skin patch tests. Our work is directed towards the development of **cultured** human skin **cells**, together with endpoints that can be linked to in vivo mechanisms of skin irritation, as in **vitro** models for prediction of human skin irritation, and for study of mechanisms of contact irritant dermatitis. Three types of commercial human skin **cell cultures** have been evaluated, epidermal keratinocytes and partially or fully cornified keratinocyte-dermal fibroblast co-cultures. Human epidermal keratinocyte cultures (Clonetics) were treated with product ingredients and formulations, and the extent of cell damage was assessed by incorporation of the vital dye neutral red. Cell damage correlated with human skin patch data for ingredient chemicals with the exception of acids and alkalis, but did not correlate with skin irritation to surfactant-containing product formulations. Cultures of human skin equivalents were evaluated as potential models for measurement of responses to test materials that could not be measured in the keratinocyte/neutral red **assay**. We developed a battery of in **vitro** endpoints to measure responses to prototype ingredients and formulations in human epidermal keratinocyte-dermal fibroblast co-cultures grown on a nylon mesh ('Skin-2' from Advanced Tissue Sciences) or on a collagen gel ('Testskin' from Organogenesis). The endpoints measure **cytotoxicity** (neutral red and **MTT** vital dye staining, **lactate dehydrogenase** and N-acetyl glucosaminidase release, glucose utilization) and inflammatory mediator (prostaglandin E-2) release. Initial experiments indicate a promising correlation between responses of the Skin-2 model to prototype surfactants and in vivo human skin irritation. The responses of Testskin cultures to acids and alkalis help to prove the concept that a topical application model can measure responses to these materials. These results suggest that human skin cell models can provide useful systems for preclinical skin irritation assessments, as alternatives to rabbits, for at least certain classes of test substances.

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TI In **vitro** and in vivo **cytotoxicity** of gossypol against central nervous system tumor cell lines.
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